This article has been accepted for publication in JME following peer review.
The definitive copyedited, typeset version is available online at 10.1136/medethics

Vaccine confidence, public understanding and probity: time for a shift in focus?

Ana Wheelock[1,2] and Jonathan Ives[3]

[1]Department of Surgery and Cancer, Imperial College London, London, UK.
[2]Business School, Kingston University, London, UK.
[3]Centre for Ethics in Medicine, Population Health Sciences, University of Bristol, UK.

Corresponding author

Dr Ana Wheelock
Address: Department of Surgery and Cancer
Imperial College London
South Kensington Campus
London SW7 2AZ, UK
Email: a.wheelock@imperial.ac.uk
Mobile: +44(0)7908373208

Keywords: vaccine, research, ethics, conflict of interest, pharmaceutical industry

Word count: 3,624

Funding

There were no external sources of funding for this research.

Acknowledgements

We would like to thank Professors Peter Openshaw (Imperial College), John Coggon (University of Bristol), Richard Huxtable (University of Bristol) and Gaëlle Vallée-Tourangeau (Kingston University), and Drs Jonathan Best (Wellcome Trust) and Gabriela Gomez (Sanofi Pasteur) for their generous advice during the conceptualisation of this research. We would also like to thank the reviewers for their valuable and constructive comments.

Competing interests

Dr Wheelock received consultancy fees from Merck UK in 2018 and Sprout Behaviour Change in 2018-2019.

Ethics approval statement

This research does not involve human participants or personal data; hence, ethics approval was not required.

Contributorship Statement

Both authors contributed equally in all stages of authorship.

Abstract

Lack of vaccine confidence can contribute to drops in vaccination coverage and subsequent outbreaks of diseases like measles and polio. Low trust in vaccines is attributed to a combination of factors, including lack of understanding, vaccine scares, flawed policies, social media, and mistrust of vaccine manufacturers, scientists and decision-makers. The Covid-19 crisis has laid bare societies' vulnerability to new pathogens and the critical role of vaccines (and their acceptability) in containing this and future pandemics. It has also put science at the forefront of the response, with several governments relying on academics to help shape policy and communicate with the public. Against this backdrop, protecting public trust in scientists and scientific output is arguably more important than ever. Yet, conflicts of interest (CoI) in biomedical research remain ubiquitous and harmful, and measures to curb them have had limited success. There is also evidence of bias in industry-sponsored vaccine studies and academics are voicing concerns about the risks of working in a CoI prevalent research area. Here, we set out to challenge established thinking with regard to vaccine confidence, by shifting the gaze from a deficit in public understanding towards probity in research relationships and suggesting an alternative and perhaps complementary strategy for addressing vaccine mistrust. We argue that a concerted effort needs to be made to revisit the norms that undergird contemporary vaccine research, coupled with a willingness of all stakeholders to reimagine those relationships with an emphasis on demonstrating trustworthiness and probity.

Introduction

Immunisation is lauded as one of the most cost-effective public health interventions and a key strategy to reduce the spread of antimicrobial resistance[1], and most recently, a critical approach to halt the Covid-19 pandemic. However, the success of this public health intervention not only depends upon how effective, accessible and safe it actually is, but also upon how it is perceived.

Vaccine confidence is a term frequently used to describe the belief that vaccines are protective, safe and part of a trustworthy medical system[2]. In the past two decades, vaccine confidence has suffered a series of setbacks [3], prompting the World Health Organization (WHO) to recognise it as one of the top ten threats to global health[4]. Low vaccine confidence is attributed to a combination of factors, including lack of understanding, vaccine scares, flawed policies, the spread of anti-vaccination messages via social media[5] and mistrust of vaccine manufacturers and decision-makers[6]. This crisis of confidence has led to drops in vaccination coverage and subsequent outbreaks of diseases like measles and polio[3,7].

Unlike therapeutic treatments aimed at curing or alleviating existing conditions, vaccines are designed to prevent a potential disease, which makes them particularly vulnerable to omission bias – the preference for harm caused by omissions (e.g. not vaccinating) over equal or lesser harm caused by acts (e.g. vaccinating)[8]. Omission bias can be exacerbated if people have reservations about the trustworthiness of the vaccine development, approval and implementation processes, especially when children's safety is at stake[9].

Challenges to vaccine confidence are global, but they are most salient in high-income countries (HICs)[10,11], where vaccines and healthcare are more accessible, vaccine-preventable diseases are less prevalent and visible, and education levels higher. The impact of this trend is illustrated by the UK's loss of its WHO 'measles-free' status[12] and France's move to make eight additional vaccines mandatory to increase uptake[13]. In adults, inaction or active vaccine refusal are more common, also resulting in inadequate coverage[14,15].

The first global survey on attitudes toward science found that low confidence in vaccines is also associated with distrust of scientists[11]. Our own analysis of this dataset revealed that only 33% of HICs participants trust 'a lot' that academic scientists seek to benefit the public and 22% trust 'a lot' that academics are honest about who funds their work[16], suggesting low overall levels of trust in academic research. Lack of trust in scientists – particularly among those who distrust vaccines – adds a new dimension to the well-established literature on the links between vaccine uptake and trust in vaccines, government and vaccine manufacturers[6,17].

The Covid-19 crisis has laid bare societies' vulnerability to new pathogens and the critical role of vaccines (and their acceptability) in containing this and future epidemics. It has also put science at the forefront of the response, with several governments relying on academics to help shape policy and communicate with the public. However, being at the frontline of a fast-moving epidemic could act as a double-edged sword. On one hand it can provide much needed expertise in support of governments' response and highlight the value of science, but on the other hand, if 'science-led' policy decisions are opaque, flawed or inappropriately executed, or if experts' independence is questioned, it can hurt the credibility of academics and their work – and concerns have been voiced by some in the academy that the rhetoric of 'science led' policy is disingenuous[18].

Against this backdrop, protecting public trust in scientists and scientific output is arguably more important than ever – and this not only requires us to take seriously and engage with peoples' concerns, but also to demonstrate trustworthiness. In the case of vaccines, however, most interventional efforts to improve vaccine confidence continue to disregard the potential legitimacy of people's concerns and focus on educating, incentivising or coercing them, with suboptimal results; the few randomised trials that have tested these approaches have shown they are minimally effective in increasing uptake and vaccine mandates have often backfired when confidence is low[2]. Notably, the behaviour of academics and vaccine manufacturers, as well as the nature and appropriateness of their relationships, remain largely under-researched and unchallenged.

In this paper, we set out to challenge established thinking with regard to vaccine confidence, by shifting the gaze from a deficit in public understanding towards probity in research relationships and proposing an alternative and perhaps complementary strategy for addressing vaccine mistrust. Our intention is not to argue this will resolve all problems or should replace other strategies, but to point towards an approach that may be fruitful. In doing so, we also posit that a perceived information/understanding deficit is unlikely to work without tackling head on the question of trust and probity.

Is a lack of trust in vaccine academics and their research reasonable?

Science studies scholars have long theorised about the ways in which publics understand and accept science, and what happens when they do not. Of particular relevance here is Wynne's argument that people cannot be expected to trust science if the integrity of the institutions that underpin it is compromised:

> "One of the general dimensions along which people experience science, and along which they can have understandings of it which scientists typically do not recognise, is that of its

> institutional structures of accountability, pluralism or hegemony, patronage, ownership and control. This logically affects the public's readiness to assimilate the contents of science"[19].

Accepting this, we propose that lack of confidence in vaccine science needs to be understood within the context of an economic and political system that consistently favours the economically advantaged, which has led to widespread dissatisfaction with the performance of democracies and low trust in the *elites*[20–22]. A prominent beneficiary of this system is the pharmaceutical industry, which in recent years has become the most profitable industry sector[23]. Their success, however, has been underpinned by unethical behaviour and aggressive tactics that have tarnished their reputation[24,25].

Integral to the pharmaceutical industry's business model are collaborations with academia, which have led to the discovery of life-saving medical technologies and treatments – and which we have relied on to develop some Covid-19 vaccines[26]. This model began to take shape during the Reagan administration in the 80s, when the US Congress passed a series of laws – notably the Bayh-Dole act[27] – to facilitate the translation of publicly funded discoveries into successful products, several of which would end up in industry's pockets[28]. Different versions of this model have been adopted elsewhere[29]. Angell points out that before this pro-business shift took place, there were two clear and separate paths for scientists; they could either "choose to live a comfortable but not luxurious life in academia, hoping to do exciting cutting-edge research or they could "sell out" to industry and do less important but more remunerative work"[24]. Since then, the interests of industry, researchers and academic institutions have become more entwined and, arguably, conflicting; and we suggest this is likely to be an important factor in public trust in vaccines.

We understand conflicts of interest as "a set of conditions in which professional judgement concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)"[30]. Although conflicts of interest do not always lead to unethical behaviour, it can compromise the integrity of academics and introduce biases that lead to harm. The insidiousness of such bias is well documented; even small gifts such as stationary or coffee can influence the behaviour of those at the receiving end, sometimes unwittingly[31].

A comprehensive report by the U.S. Institute of Medicine provided a sobering overview of how varied and ubiquitous financial conflicts of interest (for brevity, henceforth 'CoI') was in medical research[32] (see Box 1).

Box 1. Key findings from the Institute of Medicine report on conflicts of interest

- Researchers fail to disclose payments from industry.
- Unfavourable results from industry-sponsored clinical trials led by academic researchers are not published.
- Academic researchers co-author manuscripts ghost-written by industry employees that report results from studies they were not involved in.
- Researchers who develop clinical guidelines cover up their financial ties with industry.

Although there is little research on the impact of industry funding on the integrity of vaccine academics and their work, there is some indication that CoI are also prevalent and bias-inducing in this area of research. For example, 85% of vaccine clinical trials are sponsored by vaccine manufacturers and non-industry trials are over four times more likely to report negative or mixed findings than industry-sponsored trials[33]. Beutels also found that an industry-sponsored economic evaluation of vaccination scored worse in methodological appropriateness than a comparable non-industry evaluation[34].

The facts are, however, mostly irrelevant, because in matters of trust, perception is all; and it is certainly a reasonable assumption that perceived CoI in vaccine studies will impact on the trusted status of vaccine academics and trust in the science itself. An illustrative example of how the involvement of vaccine manufacturers in clinical trials and policymaking can not only sew mistrust in the science behind a particular vaccine, but also affect entire immunisation schedules, is the aftermath of the introduction of mandatory human papilloma virus (HPV) vaccination in the U.S.

Although the adoption of school mandates was hindered by multiple factors, including the newness of the vaccine and the sexual nature of HPV, Congrove and colleagues found that the involvement of the vaccine manufacturer, Merck, was particularly damaging[35]. Dismay over Merck's intervention in the policy process, including the provision of funds to an organisation of female legislators that introduced many of the bills to mandate HPV vaccination, also put in doubt the government's true motivation "to force pharmaceutical products on minors"[35]. This was quickly picked up by a prominent anti-vaccine organisation, who accused Merck of deceiving the public and concealing important safety information[36]. Strikingly, a principal investigator of HPV vaccine trials for Merck and GlaxoSmithKline agreed that "It seemed very odd to be mandating something for which 95 percent of infections never amount to anything"[37]. Further, a recent review showed that design problems in the HPV vaccine trials, most of which were led by academics but sponsored by industry, made it difficult to evaluate the extent to which the vaccine prevented cervical cancer[38]. These more recent developments are likely to increase public concern about the efficacy and safety of the HPV vaccine.

This controversy has proven contagious, not only resulting in persistent low uptake of the HPV vaccine[39], but also decreased uptake of other vaccines[35]. One response to these concerns – and a response that is typical of current models to increase vaccine uptake – is not to engage with the issues that lead to lack of trust, but to assume that lack of vaccine confidence flows from a deficit in understanding and/or that people need to be pushed into it (with varying degrees of force). These models assume the problem is lack of knowledge and/or gullible acceptance of *alternative facts*, and as such, are unlikely to be effective if the problem is in fact lack of trust because (1) the people and institutions attempting to remedy the supposed problem are the very people and institutions that are not trusted and (2) where there is no trust, attempts to nudge or coerce are likely to be strenuously resisted. Yearly (in a systematisation of empirical environmental studies) cautioned that the costs of ignoring people's concerns are high and often long-lasting[40].

The introduction of the HPV vaccine in the U.S. is one of several examples of how distrust in a vaccine, and the causes of that distrust, can have wide and perduring consequences – including the extrapolation to other vaccines, with potentially catastrophic consequences for public health[41–42], such as the recent drop in MMR vaccination in the Philippines (88% to 55%), largely due to reported risks of a new dengue vaccine[43].

Partnerships between academia and vaccine manufacturers can not only affect the trustworthiness of vaccines and vaccine science, but can also be costly for individual researchers, regardless of their discipline. In a recent commentary, a group of academics describe the "hazards" experienced by vaccine researchers, including being ostracised by peers for challenging the status quo, being attacked by anti-vaccine groups and working in a CoI prevalent research area[44]. This resonates with the experience of one of us (ID removed) and anecdotal evidence from colleagues working in vaccines, some of whom have reported feeling conflicted and stigmatised by peers for receiving industry funding.

While CoI and problems of bias in vaccine research are not new, their visibility has been significantly increased by accessible online information outlets and social networks. "Collusion" between academics and vaccine manufacturers is a common grievance among members of the public or organisations who are concerned about or against vaccines[45]. Although high-profile basic researchers are frequent targets of criticism, the integrity of social scientists can also be called into question, as illustrated in Box 2.

Despite the fact that vaccine actors are a clear source of concern about vaccines, and despite evidence of bias in industry-funded vaccine research that suggest some concern is reasonable, probity in academia-industry relationships and their impact on vaccine confidence have been largely absent from public health ethics debates. Instead, in line with much social sciences research, ethical inquiry has

centred on the behaviour of the public and the pros and cons of compulsory vaccination[46–49], with a primary focus on changing wrong behaviour, as opposed to taking seriously and addressing the (at least *prima facie* legitimate and understandable) concerns that may lead to that behaviour.

The current coronavirus epidemic is a stark reminder of the extent to which public health relies on public trust[50]. Yet, trust in public health interventions, in this case vaccines, is not formed in a vacuum; it is inextricably linked to the trustworthiness of the institutions involved in their development, approval and implementation[6,11,51]. It is, therefore, plausible that one of the reasons why containing vaccine *hesitancy* has proven so difficult is that little has been done to assuage legitimate concerns about the extent to which the motivations of experts, vaccine manufacturers and governments are aligned with the public interest.

Box 2. Examples of opinions from members of the public about vaccine researchers

Twitter exchange in response to a comment from Peter Hotez, professor of paediatrics and molecular virology and microbiology

@PeterHotez
Wow, just wow: The evidence that #vaccines DO NOT & CANNOT cause #autism is detailed in my new book @amazon https://amazon.com/Vaccines-Did-Not-Cause-Rachels-Autism/dp/1421426609. I think it's an outrage that the @thehill published this unbridled @antivax @antiscience viewpoint. Awful. #VaccinesWork

@cgammicchia
So y ou [sic] are saying the [Department of Justice's] "expert" witness was wrong? They hid the information and covered it up! Just because it's in your pro-vax book doesn't mean it's correct. Plus you have a conflict of interest on this topic don't you? #vaccinehavecausedautism

@JakeLCrosby
Petey was on @GSK's vaccine policy advisory board when he led a pro-vaccine petition against "misinformation," also around the same time @GSK stole medical records of Dr. Wakefield's patients and gave them to @DeerBrian[52]

Rapid response to an interview with Heidi Larson, professor of anthropology, risk and decision science

"It was interesting that Professor Heidi Larson expresses unease about those who take a questioning view of the vaccine industry and it's [sic] products. Many people, and I am one, have spent a professional lifetime reassuring parents that vaccines for children must be effective and safe, as the experts tell us that is so. Alarmingly, once one examines the evidence, or lack of it, that allows vaccine experts to be so confident, one discovers that the expected confirmatory evidence, for the safety and effectiveness of vaccines, is, very often, just not there… No doubt Professor Larson is aware of this, and those of us who realise that her Vaccine Confidence Project is partly funded by GSK can imagine the difficulties that conflicts of interest may cause in the amount of attention accorded to such information."[53]

O'Neill argues that trusting should not be "a matter of blind deference, but of placing – or refusing – trust with good judgement", which she refers to as "well-placed trust"[54]. We believe that vaccines are generally beneficial, although we acknowledge that not all vaccines are created equal. We also hypothesise that the public's scepticism is a reasonable response to the problems that are visible to

them in the vaccine industry and at least some lack of confidence in vaccines may be a marker of well-placed mistrust.

Protecting the integrity of medical research: why is it so difficult?

To our knowledge, no specific measures aimed at protecting the integrity of vaccine researchers and their work have been proposed or implemented. However, in the 2000s, calls led by U.S. academics to improve transparency and regulate interactions between industry, professional medical associations, academic institutions and their researchers[31,55–57] led to some positive results. For example, top academic medical centres implemented restrictions to gifts, food, honoraria, etc. originating from industry[58] and CoI began to be routinely declared in scientific journals. More recently, mandatory (U.S.) and voluntary (UK) publicly accessible registries have been created for declarations of interests between physicians (who may also work in academia) and the pharmaceutical industry[59]. These improvements in transparency, whilst certainly positive, will do little to demonstrate trustworthiness where there is already a lack of trust but, rather, such declarations will provide circumstantial evidence of reasons to withhold trust.

Meanwhile, academia-industry collaborations continue to flourish, and researchers are still encouraged by universities and funders to develop links with industry[60,61], with some expressing concerns about their reputations and income if industry support is curbed[58]. In some developed countries, the majority of panel members producing clinical practice guidelines have disclosed or undisclosed financial CoI[62].

A similar trend can be observed in vaccine research[63], including Covid-19 vaccines[64]. Current events aside, in the UK, for example, a government-backed vaccine network is bringing closer together industry, academia and relevant funding bodies to make targeted investments in vaccines and vaccine technology[65]. Consequently, all aspects of most high impact, industry-sponsored clinical trials remain influenced by industry[66] and systematically produce more favourable efficacy findings and conclusions than research supported by other sources[32,67].

With plenty of evidence showing how the pharmaceutical industry has directly (e.g. biased research) or indirectly (e.g. mistrust) threatened public health[68,69], unregulated academia-industry relationships have the potential to inflict further damage during the Covid-19 pandemic and in years to come. This is because vigorous and urgent efforts to develop and produce Covid-19 treatments and vaccines, without appropriate and highly visible safeguards against conflicts of interest, could not only multiply and consolidate academia-industry relationships, but also fuel existing distrust in vaccine candidates. There is already some indication that the acceptability of Covid-19 vaccines may not be as high as we hoped. In recent polls, only 29% of people in the U.S. said they would definitely take the vaccine,

almost a third did not intend to vaccinate and were "pretty" certain that more information will not change their mind, and intention to vaccinate was linked to confidence in the research and development process[70]. In the UK, over a third of people said they were unlikely to vaccinate and 48% felt concerned about safety[71], and intention to refuse the vaccine was linked to beliefs and perceptions reflecting scepticism about scientific experts and government[72].

An obvious reason why it has been so difficult to curtail CoI, is that there is no consensus among academic institutions about how to manage it[73]. This is reflected in substantial variability in the contents and detail of institutional CoI policies (when one is available), and the way these policies are enforced[74]. Notably, most CoI policies focus on disclosure rather than prevention.

This *ad hoc* and light touch approach to CoI, however, is likely to be influenced by a constellation of often interrelated factors. Given the lack of agreement about how to manage CoI and how normalised academia-industry partnerships are, it is perhaps unsurprising that many academics are still confused about what relationships constitute CoI and appear to have limited knowledge about why they may be morally contestable[75]. Some argue that academic institutions have little incentive to regulate CoI, when the revenue generated by their partnerships with industry is so significant[76]. Others believe that the focus on disclosure in the medical sciences may confer on physicians and researchers a kind of moral immunity that exempts them from their duty to deal with the issues raised by CoI[77]. Thacker suggests that "many scientists are incapable of understanding and accepting that financial conflicts of interest corrupt science because they believe that scientists are objective and too well trained to be influenced by financial rewards, like all other human beings"[78].

Can the trustworthiness of vaccine science be improved?

CoI in biomedical research is a complex and pervasive problem. Whilst CoI are not only caused by academia's relationships with industry, it is safe to say that these ties, in their current form, are a significant source of misconduct and mistrust[45,67,68]. The relationships between academics and vaccine manufacturers are particularly problematic, not only because they threaten the integrity of academics and science, but critically because they erode public trust in vaccines and put public health at risk.

Certainly, overreliance on transparency (i.e. declaring CoI) as a strategy to improve trustworthiness has not been very effective. O'Neill suggests that one reason why public distrust has grown in an era of openness, is the realisation that transparency may not curtail intentional misinformation that weakens relations of trust, and that it is the risk of deception, not lack of transparency, that is the real enemy of trust[54]. Transparency, albeit desirable, is not only insufficient to curb deception, but may also provide cover for it. Braillon rightly reminds us that transparency is just a tool, independence should be the goal[79]. Angell[24] and, more recently, Moynihan and colleagues[80] have proposed

evidence-based and actionable pathways to disentangle academia from commercial interests, which warrant careful consideration (Box 3). Cutting ties between industry and other key actors, such as government authorities and regulatory agencies, may help to improve vaccine confidence, but the arguments for this will be complex and are outwith what we can achieve in this paper.

Given the lack of public debate about the need to improve the trustworthiness of vaccine research, or consensus about how to do it, there seems to be an obvious need to create a platform for public deliberation on the issue and to conduct high quality empirical research to explore trust and trustworthiness in vaccine development, and their impact on vaccine uptake. Understanding the problem holistically is an essential first step towards addressing it, and we suggest that one of the reasons that most contemporary attempts to address vaccine *hesitancy* have had limited effectiveness

Box 3. Possible strategies to cut ties between academia and industry

- Governments require that evidence used for healthcare decision making is independently produced and all public healthcare organisations and their advisers (who may also be academics) have no financial relationships with industry[80].
- Groups producing research syntheses provide reviewers with all available information on study methods and results and should be conducted without industry funding and by authors with no conflicts of interest[80].
- Academic groups engaged in educational activities for health professionals or the public, or advocacy influencing regulatory or policy decisions, sever financial ties with industry[80].
- Medical journals and their editors sever financial ties with industry[80].
- Research funding agencies and academic institutions modify metrics and incentives to reward academic collaboration with public agencies and civil society[80].
- An independent institute within a public research funding agency is created to administer clinical trials and act as an intermediary between academia and industry[24].

is the deep-rooted assumption that it is the behaviour of the public that needs changing, not the individual and collective behaviour of those charged with developing, approving, manufacturing, recommending and distributing vaccines. This is not to suggest that they systematically act wrongly – rather, that they do not take explicit and effective steps to demonstrate trustworthiness. A concerted effort, then, needs to be made to revisit the norms that undergird contemporary vaccine research, coupled with a willingness of all stakeholders to reimagine those relationships with an emphasis on demonstrating trustworthiness and probity.

This discussion has inexorably transformed into a call to address a deficit in the research agenda – and turn a critical gaze on the relationships between the actors that seem to have the most to gain from maintaining the status quo. The ethical imperative for doing so is, we hope, now clear. The status quo does not serve the public interest, and as long as it engenders mistrust, it threatens confidence in, and therefore the success of, one of our most effective public health measures.

We acknowledge that protecting the integrity of vaccine researchers and their work will take significant resolve and effort, and possibly a paradigm shift in how academia and industry relate to each other. Yet, in these turbulent times, where ‘unprecedented’ is a term routinely wielded, a serious questioning of science’s institutional structures of accountability, pluralism or hegemony, patronage, ownership and control may be possible.

REFERENCES

1 World Health Organization. *Why is vaccination important for addressing antibiotic resistance?* 2016. https://www.who.int/features/qa/vaccination-antibiotic-resistance/en/ (accessed 12 August 2020).

2 Brewer NT, Chapman GB, Rothman AJ, *et al.* Increasing vaccination: putting psychological science into action. *Psychological Science in the Public Interest* 2017;**18**:149–207.

3 World Health Organization. *2018 assessment report of the Global Vaccine Action Plan*. Geneva: Strategic Advisory Group of Experts on Immunization. 2018. https://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2018_EN.pdf (accessed 12 August 2020).

4 World Health Organization. *Ten threats to global health in 2019*. 2019. https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019 (accessed 10 December 2020).

5 Kennedy J. Populist politics and vaccine hesitancy in Western Europe: an analysis of national-level data. *Eur J Public Health* 2019;**29**:512–516.

6 Larson HJ, Jarrett C, Eckersberger E, *et al.* Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of published literature, 2007–2012. *Vaccine* 2014;**32**:2150–2159.

7 UNICEF. Leaving no one behind - All children immunized and healthy. New York: UNICEF. 2019. https://www.unicef.org/media/55706/file/UNICEF_Leaving_No_One_Behind_Immunization_2019.pdf (accessed 12 August 2020).

8 Ritov I, Baron J. Reluctance to vaccinate: Omission bias and ambiguity. *J Behav Decis Making* 1990;**3**:263–277.

9 Brown KF, Kroll JS, Hudson MJ, *et al.* Omission bias and vaccine rejection by parents of healthy children: implications for the influenza A/H1N1 vaccination programme. *Vaccine* 2010;**28**:4181–4185.

10 Larson HJ, Schulz WS, Tucker JD, *et al.* Measuring vaccine confidence: introducing a global vaccine confidence index. *PLoS Currents* 2015;**7**.

11 Wellcome Trust and Gallup. *Wellcome Global Monitor - How does the world feel about science and health?* London: Wellcome Trust. 2018. https://wellcome.ac.uk/reports/wellcome-global-monitor/2018 (accessed 12 August 2020).

12 Public Health England. *Measles in England. Public health matters*. 2019. https://publichealthmatters.blog.gov.uk/2019/08/19/measles-in-england/ (accessed 12 August 2020).

13 Ward JK, Colgrove J, Verger P. Why France is making eight new vaccines mandatory. *Vaccine* 2018;36(14):1801-3.

14 Bricout H, Torcel-Pagnon L, Lecomte C, *et al.* Determinants of shingles vaccine acceptance in the United Kingdom. *PloS One* 2019;**14**:e0220230.

15 Wheelock A, Miraldo M, Thomson A, *et al.* Evaluating the importance of policy amenable factors in explaining influenza vaccination: a cross-sectional multinational study. *BMJ open* 2017;**7**:e014668.

16 Wellcome Trust and Gallup. *Wellcome Global Monitor 2018 dataset and cosstabs for all countries*. 2018. https://wellcome.ac.uk/reports/wellcome-global-monitor/2018 (accessed 12 August 2020).

17 Freimuth VS, Jamison AM, An J, *et al.* Determinants of trust in the flu vaccine for African Americans and Whites. *Soc Sci Med* 2017;**193**:70–79.

18 Fritz Z, Huxtable R, Ives J, *et al.* Ethical road map through the covid-19 pandemic. *BMJ* 2020;**369**:m2033

19 Wynne B. Public uptake of science: a case for institutional reflexivity. *Public Underst Sci* 1993;**2**:321–337.

20 Buttrick NR, Oishi S. The psychological consequences of income inequality. *Soc Personal Psychol Compass* 2017;**11**:e12304.

21 Stiglitz J. *People, power, and profits: Progressive capitalism for an age of discontent*. United Kingdom: Allen Lane, 2019.

22 Foa RS, Klassen A, Slade M, *et al. Global Satisfaction with Democracy 2020*. Cambridge: Centre for the Future of Democracy. 2020. https://www.bennettinstitute.cam.ac.uk/media/uploads/files/DemocracyReport2020.pdf (accessed 12 August 2020).

23 Dickson S and Ballreich J. *How Much Can Pharma Lose? A Comparison of Returns Between Pharmaceutical and Other Industries*. Washington D.C.: West Health Policy Center & Johns Hopkins Bloomberg School of Public Health. 2019. https://www.westhealth.org/wp-content/uploads/2019/11/WHPC_White-Paper_How-Much-Can-Pharma-Lose_FINAL-November-2019.pdf (accessed 12 August 2020).

24 Angell M. *The truth about the drug companies: How they deceive us and what to do about it*. New York: Random House, 2005.

25 Bauchner H and Fontanarosa PB. Restoring confidence in the pharmaceutical industry. *JAMA* 2013;**309**:607–609.

26 Gallagher J. *Covid vaccine update: When will others be ready?* BBC. 8 December 2020. https://www.bbc.co.uk/news/health-51665497 (accessed 9 December 2020).

27 U.S. General Accounting Office. *Technology Transfer: Administration of the Bayh-Dole Act by Research Universities (GAO/RCED-98-126)*. Washington, D.C.: 1998. https://www.gao.gov/archive/1998/rc98126.pdf (accessed 12 August 2020).

28 Kenney M, Patton D. Reconsidering the Bayh-Dole Act and the current university invention ownership model. *Res Policy* 2009;**38**:1407–1422.

29 Mowery DC, Sampat BN. The Bayh-Dole Act of 1980 and university–industry technology transfer: a model for other OECD governments? *J Technol Transf* 2005;**30**(1):115-27.

30 Thompson DF. Understanding financial conflicts of interest. *NJME* 1993;**329**:573–573.

31 Katz D, Caplan AL, Merz JF. All gifts large and small: toward an understanding of the ethics of pharmaceutical industry gift-giving. *Am J Bioethics* 2010;**10**:11–17.

32 Institute of Medicine. *Conflict of Interest in Medical Research, Education, and Practice*. Washington, D.C.: The National Academies Press, 2009.

33 Manzoli L, Flacco ME, D'Addario M, *et al.* Non-publication and delayed publication of randomized trials on vaccines: survey. *BMJ* 2014;**348**:g3058.

34 Beutels P. Potential conflicts of interest in vaccine economics research: a commentary with a case study of pneumococcal conjugate vaccination. *Vaccine* 2004;**22**:3312–3322.

35 Colgrove J, Abiola S, Mello MM. HPV vaccination mandates—lawmaking amid political and scientific controversy. *NEJM* 2010;**363**:785–791.

36 Children's Health Defense. *Merck Accused of Fraud, Deceit and Negligence in US Gardasil Case*. 2018. https://childrenshealthdefense.org/news/merck-accused-of-fraud-deceit-and-negligence-in-us-gardasil-case/ (accessed 12 August 2020).

37 Knox R. HPV vaccine: *The science behind the controversy*. Morning edition: your health. 2011. https://www.npr.org/2011/09/19/140543977/hpv-vaccine-the-science-behind-the-controversy?t=1595326098455 (accessed 12 August 2020).

38 Rees CP, Brhlikova P, Pollock AM. Will HPV vaccination prevent cervical cancer? *J R Soc Med* 2020;113:**2**:64–78.

39 Conrey R, Valencia V, Cioletti A, *et al.* Regional variation in human papillomavirus vaccination uptake and completion among adolescents 13–17 in the state of Texas. *Vaccine* 2020;**38**: 4119-4124.

40 Yearley S. *Cultures of environmentalism: Empirical studies in environmental sociology*. United Kingdom: Palgrave Macmillan, 2005.

41 Peretti-Watel P, Verger P, Raude J, *et al.* Dramatic change in public attitudes towards vaccination during the 2009 influenza A (H1N1) pandemic in France. *Eurosurveillance* 2013;**18**:20623.

42 Burgess DC, Burgess MA, Leask J. The MMR vaccination and autism controversy in United Kingdom 1998–2005: Inevitable community outrage or a failure of risk communication? *Vaccine* 2006;**24**:3921–3928.

43 Dyer O. Philippines measles outbreak is deadliest yet as vaccine scepticism spurs disease comeback. *BMJ* 2019;364:l739.

44 Bragazzi NL, Watad A, Amital H, *et al.* Debate on vaccines and autoimmunity: do not attack the author, yet discuss it methodologically. *Vaccine* 2017;**35**:5522–5526.

45 Moran MB, Lucas M, Everhart K, *et al.* What makes anti-vaccine websites persuasive? A content analysis of techniques used by anti-vaccine websites to engender anti-vaccine sentiment. *J Health Commun* 2016;**9**:151–163.

46 Colgrove J. The ethics and politics of compulsory HPV vaccination. *NEJM* 2006;**355**:2389–2391.

47 Dawson A. The moral case for the routine vaccination of children in developed and developing countries. *Health Aff* 2011;**30**:1029–1033.

48 Gostin LO, Ratzan SC, Bloom BR. Safe Vaccinations for a Healthy Nation: Increasing US Vaccine Coverage Through Law, Science, and Communication. *JAMA* 2019;**321**:1969–1970.

49 Hendrix KS, Sturm LA, Zimet GD, *et al.* Ethics and childhood vaccination policy in the United States. *Am J Public Health* 2016;**106**:273–278.

50 Wynia MK. Public health, public trust and lobbying. *Am J Bioethics* 2007;**7**:4–7.

51 Attwell K, Leask J, Meyer SB, *et al.* Vaccine rejecting parents' engagement with expert systems that inform vaccination programs. *J Bioeth Inq* 2017;**14**:65–76.

52 Hotez P. Wow, just wow: The evidence that #vaccines DO NOT & CANNOT cause #autism is detailed in my new book […]. [Twitter]. 13 Jan 2019. https://twitter.com/peterhotez/status/1084491317680525313 (accessed 13 May 2020).

53 Thomas, N. Re: Overcoming vaccine hesitancy: Five minutes with... Heidi Larson. 30 March 2019. https://www.bmj.com/content/364/bmj.l1259/rr-4 (accessed 13 May 2020).

54 O'Neill O. *A question of trust: The BBC Reith Lectures 2002*. Cambridge: Cambridge University Press, 2002.

55 Brennan TA, Rothman DJ, Blank L, *et al.* Health industry practices that create conflicts of interest: a policy proposal for academic medical centers. *JAMA* 2006;**295**:429–433.

56 Korn D. Conflicts of interest in biomedical research. *JAMA* 2000;**284**:2234–2237.

57 Rothman DJ, McDonald WJ, Berkowitz CD, *et al.* Professional medical associations and their relationships with industry: a proposal for controlling conflict of interest. *JAMA* 2009;**301**:1367–1372.

58 Rothman DJ, Chimonas S. Academic medical centers' conflict of interest policies. *JAMA* 2010;**304**:2294–2295.

59 Dunn AG, Coiera E, Mandl KD, *et al.* Conflict of interest disclosure in biomedical research: a review of current practices, biases, and the role of public registries in improving transparency. *Res Integr Peer Rev* 2016;**1**:1.

60 National Institutes of Health. NIH-Industry Partnerships Frequently Asked Questions. https://ncats.nih.gov/ntu/about/partnerships-faq (accessed 13 May 2020).

61 National Institute for Health Research. Partners and industry. https://www.nihr.ac.uk/partners-and-industry/ (accessed 13 May 2020).

62 Neuman J, Korenstein D, Ross JS, *et al.* Prevalence of financial conflicts of interest among panel members producing clinical practice guidelines in Canada and United States: cross sectional study. *BMJ* 2011;**343**:d5621.

63 National Vaccine Advisory Committee. United States vaccine research: a delicate fabric of public and private collaboration. *Pediatrics* 1997;**100**(6):1015–20.

64 Mahase E. Covid-19: UK agrees "early access" deal with companies to get 90 million vaccine doses. *BMJ* 2020;**370**:m2914.

65 Department of Health and Social Care. UK Vaccine Network. https://www.gov.uk/government/groups/uk-vaccines-network (accessed 13 May 2020).

66 Rasmussen K, Bero L, Redberg R, *et al.* Collaboration between academics and industry in clinical trials: cross sectional study of publications and survey of lead academic authors. *BMJ* 2018;**363**:k3654.

67 Lundh A, Lexchin J, Mintzes B, *et al.* Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2017;**2**:MR000033.

68 Krimsky S. *Conflicts of Interest in Science: How Corporate-Funded Academic Research Can Threaten Public Health*. New York: Simon and Schuster, 2019.

69 Marks JH. *The perils of partnership: Industry influence, institutional integrity, and public health*. Oxford: Oxford University Press, 2019.

70 Funk C and Alex T. *Intent to Get a COVID-19 Vaccine Rises to 60% as Confidence in Research and Development Process Increases*. Pew Research Center. 3 December 2020.

https://www.pewresearch.org/science/2020/12/03/intent-to-get-a-covid-19-vaccine-rises-to-60-as-confidence-in-research-and-development-process-increases/ (accessed 9 December 2020).

71 Michael Savage. *One in three 'unlikely to take Covid vaccine'*. The Guardian. 6 December 2020. https://www.theguardian.com/world/2020/dec/06/one-in-three-unlikely-to-take-covid-vaccine (accessed 9 December 2020).

72 Duffy, Bobby. *Coronavirus uncertainties: vaccines, symptoms and contested claims*. London: The Policy Institute, King's College London. 2020. https://www.kcl.ac.uk/policy-institute/assets/coronavirus-uncertainties.pdf (accessed 12 August 2020).

73 Shamoo AE, Resnik DB. *Responsible conduct of research*. Oxford: Oxford University Press, 2015.

74 Resnik DB. Institutional conflicts of interest in academic research. *Sci Eng Ethics* 2015;1–9.

75 Aytug ZG, Rothstein HR, Kern MC, *et al.* Is There Social Consensus Regarding Researcher Conflicts of Interest? *Ethics Behav* 2019;**29**:101–140.

76 Boyd EA and Bero LA. Assessing faculty financial relationships with industry: a case study. *JAMA* 2000;**284**:2209–2214.

77 Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. *JAMA* 2012;**307**:669–670.

78 Thacker PD. Transparency and Conflicts in Science: History of Influence, Scandal, and Denial. In Çalıyurt K ed. *Integrity, Transparency and Corruption in Healthcare & Research on Health, Volume I*. Singapore: Springer Nature, 2020:3–26.

79 Braillon A. Transparency or Independence in Conflict of Interest Disclosures. *JAMA Oncol* 2016;**2**:1661.

80 Moynihan R, Bero L, Hill S, *et al*. Pathways to independence: towards producing and using trustworthy evidence. *BMJ* 2019;**3**:367.